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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,933	12/31/2003	Dilip G. Saoji	U 014338-7	6675

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
02/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/749,933	SAOJI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-50 and 52-55* is/are pending in the application.

4a) Of the above claim(s) *22-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-50 and 52-55* is/are rejected.

7)☒ Claim(s) *38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/5/07 has been entered.

The response filed **11/5/07** presents remarks and arguments to the office action mailed **10/24/07**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 22-50 and 52-55 are pending, claims 22-37 are withdrawn and claim 51 is cancelled.

Claims 38-50 and 52-55 are acted upon in this office action.

Claim Objections

Claim 38 is objected to because of the following informalities: There are Therefore one of ordinary skill in the art would have known to combine many “or” in the claim, see page 6, line 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-50 and 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear whether "a non-steroid,” is separate from “anti-inflammatory agent” and “a non-steroid anti-inflammatory agent.

Maintained Claim Rejections - 35 USC § 103

Applicant is arguing that the below cited references do not teach or suggest that the compounds of claims 38-45 and 54-55 can be into a single composition.

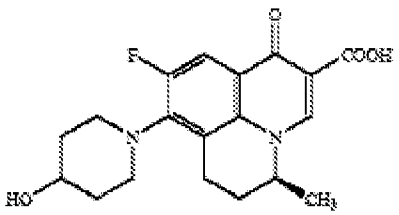
In response, the argument is found not persuasive. The claims recite the compounds of instant claims 38-39 etc, the deSousa reference teaches the compound. The claims recite in combination with other pharmaceutical effective amounts of a retinoid, non-steroid anti-inflammatory agents. The deSousa reference teaches the

pharmaceutical formulation can be combined with other active agents such as antibacterial agents. Even though the reference do not teach the agents claimed by Applicant it teaches us that other drugs other than antibacterial can be used. Col. 8, lines 29-34 teaches that other active agents are capable of been added to the pharmaceutical formulation. Also the office action provides reasons why one would combine the prior art. With regards to the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

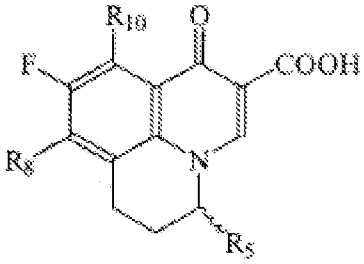
The argument is found not persuasive and the rejection is maintained below.

Claims **38-45 and 54-55** remain rejected under 35 U.S.C. 103(a) as being obvious over de Souza et al. US 6,514,986 in view of de Souza et al. US 6,608,078 B2 taken with Leyden J. Euro. Academy of dermatology and venereology15 (suppl.3). 51-55.

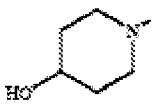
De Souza et al. ('986) teach a stable pharmaceutical composition comprising an aqueous carrier having in solution therein a benzoquinolizine-2-carboxylic acid



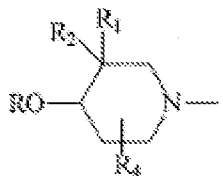
having the core chemical structure



as that disclosed in the instant claim 38 (see col. 4, lines 15+) that is an optical active isomer, in a pharmaceutically acceptable salt arginine singly or combined with other active agent such as antibacterial agents (see col. 8, lines 32+). Please not after making the substitution the deSousa compound is obvious as shown above. For example R_5 is CH_3, R_8 is the substitution



and R_{10} is hydrogen clearly depicted by the compound of deSousa. Note, the reference did not teach using any particular drug combination as cited in claim 38. , With regards to R_5 is CH_3 (C=1) and R8 is



is shown in the above structure, where R_1, R_2 R_4 are hydrogen. As to claims 39 and 40-41 the

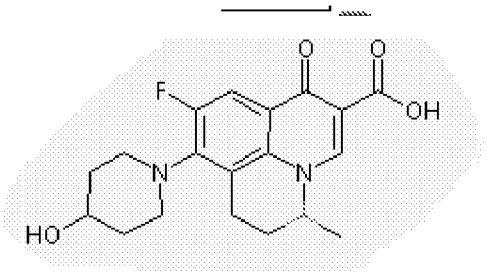
benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin- 1-yl)-5-methyl- 1-oxo- 1H,5H- benzo(ij)quinolizine-2-carboxylic acid (see abstract) the drug is used to treat antimicrobial infection and the arginine salt form in claim 4 (see col. 5 lines 20+), wherein the pharmaceutically acceptable salt if from an acid (see col. 2, lines 1+) as in claim 55 having a physical form of a cream (see col. 8, lines 35+)as in claim 21.

The reference teaches ('078) a stable pharmaceutical composition having the core structure of the claimed invention (see col. 5, lines 25+), wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin- 1-yl)-5-methyl- 1-oxo- 1H,5H- benzo(ij)quinolizine-2-carboxylic acid and the arginine salt form in claims 38-41 (see col. 8 lines 11+) wherein the pharmaceutically acceptable salt is from an acid (see col.6 lines 65+). The reference further teaches having a physical form of a cream (see col. 14, lines 1+) as in claim 55. The reference teaches addition of inorganic basic salts (see col. 6, line 55-57) as in the instant claim 54. With regard to the polymorphic forms as required by instant claim 40 is taught. See col. 4, lines 41-43.

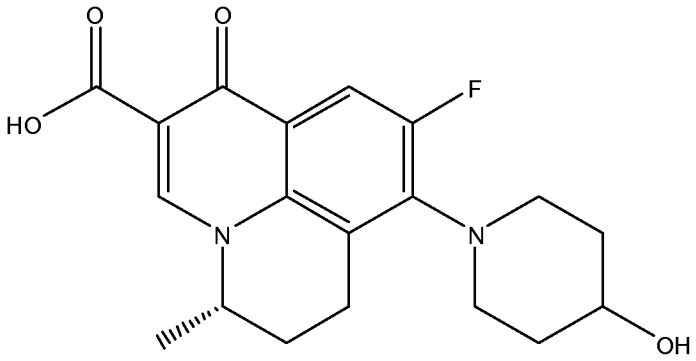
As to claims 42-44, the reference teaches the benzoquinolizine –2- carboxylic acid comprises 0-1 to 10% of the compound (see col. 15, lines 1-6).

The reference also teaches the compounds can be combined with other ingredients such as antimicrobial agents. See col. 8, lines 32-33. Clearly suggesting to one of ordinary skill in the art based on the use or disease symptom, other types of active ingredients can be used. However, did not clearly state it.

Leyden teaches that antimicrobial agents nadifloxican-



(same drug as the claimed compound



S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin- 1-yl)-5-methyl- 1-oxo- 1H,5H- benzo(ij)quinolizine-2-carboxylic acid

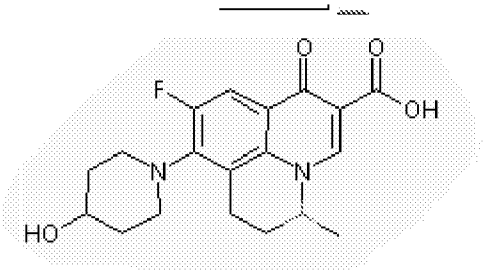
Caution: Stereochemical terms discarded: -

) are used in combination therapy with retinoids as in claim 45 (see abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the above taught composition for the purpose of treating microbial infections (microbial infection such as fugal infection) having the above-cited reference and include a retinoid to the said formulation as an adjuvant therapy because it is known in the art that retinoids are used in medicine, primarily due to the way they regulate epithilial cell growth especially in the regulation of cell proliferation in inflammatory skin disease. Although, the combined references did not expressly state the kind of retinoid agent to be used, one of ordinary skill in the art would be motivate to choose any of the retinoid agents in the claimed invention as

expect a successful result in doing so because these agents are well know as antimicrobial agents and have been used in many formulation. Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Claims **45 and 51-52** are rejected under 35 U.S.C. 103(a) as being obvious over de Souza et al. US 6,514,986 taken with de Souza et al. US 6,608,078 B2 in view Leyden J. Euro. Academy of dermatology and venereology15 (suppl.3). 51-55 as applied to claims **38-45 and 54-55** above, and further in view of Katsambas et al. Clinics in Dermatology 2000; 18:171-176.

Katsamnas et al. teach treatment indications of acne, perioral dermatitis, wherein antimicrobials have been used-thus the claimed compound is an antimicrobial drug (nadifloxacin- 

(see page 171-highlighted), anti-inflammatory agents (see page 171-highlighted), retinoids (isotretinoin as in claim 45 see page 172-highlighted), antifungal agents such as ketoconazole as in claims 51-52 (see page 172-highlighted) and steroids as hormones all have been used to treat acne.

The reference did not however teach the use together, but Leydon teaches that the compound is used with a retinoid agent for the treatment of dermatological diseases, therefore, one of ordinary skill in the art would be motivated to use agents that have been known to individually treat the same disease condition.

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07. Examiner notes that the particular drugs in claims 46, 47-50 and 53 are not taught, however, one of ordinary skill in the art would be motivated to use any of the retinoid or other antifungal or anti-inflammatory agents based on t6he condition of the patient. Absence factual evidence, if the disease (acne) is accomplished with pain or fever, it is well within the level of one ordinary ski8ll in the art to administer a pain medication together with the drug, based on the fact that the drug has been used with other types of drugs, therefore would expect a successful result of the treatment. Substituting one retinoid with another would be obvious because one of ordinary skill in the art would expect the function of the retinoid to be the same.

No claim is allowed .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
1/30/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614